1.0 EXECUTIVE SUMMARY

The purpose of this report is to provide a firm basis for completing a state-of-the-art-protocol to assess potential human-health risks associated with exposure to asbestos. Such a protocol is intended specifically for use in performing risk assessments at Superfund sites, although it may be applicable to a broad range of situations.

The approach currently employed at the U.S. Environmental Protection Agency (U.S. EPA) to evaluate asbestos-related risks (IRIS 1988) is based primarily on a document completed in 1986 (U.S. EPA 1986) and has not been changed substantially in the past 15 years, despite substantial improvements in asbestos measurement techniques and in the understanding of the manner in which asbestos exposure contributes to disease. Therefore, this document provides an overview and evaluation of the more recent studies and presents proposed modifications to the protocol for assessing asbestos-related risks that can be justified based on the more recent work.

The studies relevant to developing a protocol are reviewed in this document and combined with supporting analysis to resolve issues and identify the best candidate procedures for assessing asbestos-related risks. Although the objective of this evaluation was to identify the single best procedures, when current knowledge is inadequate for distinguishing among alternatives, options are presented along with a discussion of their relative advantages and limitations. In a few cases, limited and focused additional research studies are recommended, which may enhance the current state of knowledge sufficiently to resolve one or more of the important, remaining issues.

Inhalation of asbestos dusts has been linked to several adverse health effects including primarily asbestosis, lung cancer, and mesothelioma (U.S. EPA 1986). Asbestosis, a chronic, degenerative lung disease, has been documented among asbestos workers from a wide variety of industries. Although asbestosis cases have been observed at some locations of current interest to the U.S. EPA, the disease is generally expected to be associated only with the higher levels of exposure commonly found in workplace settings and is not expected to contribute substantially to potential risks associated with environmental asbestos exposure. Therefore, asbestosis is only considered in this document to the extent required to address it's putative association with lung cancer. Overall, the majority of evidence indicates that lung cancer and mesothelioma are the most important sources of risk associated with exposure to low levels of asbestos.

A variety of human, animal, and tissue studies have provided insight into the nature of the relationship between asbestos exposure and disease. Ideally, human epidemiology studies are employed to determine the quantitative dose/response relationships and the attendant risk coefficients for asbestos exposure. Risk coefficients have been estimated for asbestos from approximately 20 epidemiology studies for which adequate

dose-response data exist. Such factors vary widely, however, and the observed variation has not been reconciled. Among the objectives addressed in this study is to evaluate and account for the sources of uncertainty that contribute to the variation among the risk coefficients derived from the literature so that these estimates can be reasonably interpreted and recommendations for their use in risk assessment developed.

Animal and tissue studies indicate that asbestos potency is a complex function of several characteristics of asbestos dusts including fiber size and fiber type (i.e., fiber mineralogy). Moreover, the influence of fiber size is a complex function of both diameter and length as critical parameters (among others). Therefore, whenever the goal is to compare across samples with differing characteristics, it is not sufficient to report asbestos concentrations simply as a function of mass (or any other single parameter) and this stands in stark contrast to the treatment of chemical toxins. It has generally been difficult to distinguish among the effects of fiber size and type in many studies because such effects are confounded and the materials studied have not been adequately characterized. However, several adequate studies do exist and these have been highlighted.

The influence of such effects cannot be adequately evaluated in the existing epidemiological studies because the analytical techniques used to monitor asbestos exposure in these studies are not capable of resolving all of the characteristics of asbestos dusts that other studies indicate are important. Moreover, the exposure indices (the range of structure sizes and shapes included in an analysis) that are employed in the existing epidemiology studies may not correspond precisely with the characteristics of asbestos that best relate to biological activity. This hinders the ability to compare the risk (dose-response) coefficients derived from the different studies. It also limits the confidence with which risk coefficients derived from the existing epidemiology studies can be applied to assess risks from asbestos exposure in other environments. Such limitations are explored in this study, along with potential remedies. At the same time, the existing epidemiology studies provide the most appropriate data from which to determine the relationship between asbestos dose and response in humans.

Briefly, the major kinds of limitations that potentially contribute to uncertainty in the available epidemiology studies (and the effect such limitations likely produce on trends in potency estimates) include:

- limitations in the manner that exposure concentrations were estimated (likely increases random variation across studies);

- limitations in the manner that the character of exposure (i.e. the mineralogical types of fibers and the range and distribution of fiber dimensions) was delineated (likely increases systematic variation between industry types and, potentially, between fiber types);

- limitations in the accuracy of mortality determinations or incompleteness in the extent of tracing of cohort members (likely increases random variation across studies);

- limitations in the adequacy of the match between cohort subjects and the selected control population (likely increases random variation across studies and may have a substantial effect on particular studies); and

- inadequate characterization of confounding factors, such as smoking histories for individual workers (likely increases random variation across studies and may have a substantial effect on particular studies).

Importantly, this new analysis of the epidemiology database differs from the evaluation conducted in the 1986 Health Effects Assessment Update (U.S. EPA 1986). Not only does it incorporate studies containing the latest available followup for the exposure settings previously evaluated and several additional studies addressing new exposure settings, but the manner in which the analysis was conducted incorporates important, new features including estimation of more realistic confidence bounds for the dose-response factors derived from each study.

Confidence bounds were adjusted to account for uncertainty contributed by the manner that exposure was estimated, by the manner that work histories were assigned, and by limitations in the degree of followup, in addition to the traditional practice of accounting for the statistical uncertainty associated with the observed incidence of disease mortality. Thus, most of the major contributors to the overall uncertainty of each study are now addressed, at least in qualitative fashion. By better accounting for overall uncertainty, we were better able to distinguish what can and cannot be reasonably concluded from the existing studies.

Separately, we also completed an evaluation to consider questions concerning the appropriateness of the range of fiber sizes characterized in the published epidemiology studies and whether adjusted exposure indices might improve the quality of asbestos risk assessments. This was motivated by conclusions from our review of the supplemental literature, which indicate that the methods used to assess exposure in the existing epidemiology studies do not adequately reflect the characteristics of asbestos that determine biological activity.

Results from our evaluation of the available epidemiology studies indicate that:

(1) the results of individual epidemiology studies are uncertain, especially when one considers all of the major potential sources of uncertainty (rather than simply considering the statistical uncertainty associated with the number of deaths, as is traditionally done). However, more robust conclusions can be drawn from an analysis of the set of epidemiology studies taken as a whole than results derived from individual studies;

(2) by adjusting for fiber size and fiber type, the existing database of studies can be reconciled adequately to reasonably support risk assessment;

(3) the procedures recommended as a result of our analysis offer substantial improvement over EPA's current approach to evaluating asbestos-related risks;

(4) while there is some indication that the existing EPA models for lung cancer and, potentially, mesothelioma may not entirely reflect the time-dependence of disease at long times following cessation of exposure, such effects appear to be modest so that they are unlikely to adversely affect the proposed approach. Prudence dictates, however, that limited additional study may be warranted to adequately dismiss related concerns; and

(5) results from our review of the supplemental literature provide additional support for the approach recommended in this document and indicate additional, specific modifications that (if supported by limited additional study) could result in substantial improvement even over the approach currently recommended, which (in turn) provides substantial improvement over the current approach.

Based on our analysis, we recommend the following.

(1) Asbestos concentrations should be analyzed for structures that correspond to a new (interim) exposure index that is defined in this document. As previously indicated, an exposure index is a description of the sizes and shapes of fibers (and the relative weights to be assigned to each category of size and shape) that need to be counted in an analysis to determine asbestos concentrations.

(2) Because amphiboles, fiber-for-fiber, were found to be substantially more potent than chrysotile, the individual contributions from chrysotile and the combined amphiboles to any particular exposure need to be separately delineated and, because amphibole exposures are the primary drivers, the analytical sensitivity required for each particular study should be set based on amphiboles.

A set of new dose-response coefficients for chrysotile and the amphiboles are also recommended in this document, which indicate the relative potency of each toward the induction of lung cancer and mesothelioma, respectively.

Three options are presented in this document for incorporating the new exposure index, the new dose-response coefficients, and the other recommendations in this document into a general protocol for assessing asbestos-related risks:

- the first option involves performing lifetable analyses using the dose-response models that EPA currently recommends for lung cancer and mesothelioma. When sufficient data are available from a particular project to support this type of analysis, it should provide the best site-specific estimates of asbestos-related risks;

- the second option involves use of a risk table, which can be adapted to estimate risk for most cases of interest, even ones for which exposure estimates are crude and descriptions of the circumstances of exposure are sparse; and

- the third option involves development of a new unit risk factor for asbestos (based on the latest data presented in this document), which would replace the unit risk factor in current use.

A couple of focused, additional studies are also recommended in this document, due to a small number of important knowledge gaps that remain to be resolved, that can be resolved cost-effectively, and that, if resolved, can substantially increase both the overall confidence in the proposed approach and, potentially, improve the approach as well. Importantly, even without conducting the new studies, the approach currently recommended was shown in this document to provide substantial improvement in the ability to assess asbestos-related risks (in terms of reducing error) over the approach in current use. The objectives of the proposed studies are:

(1) to expand the test of the ability of the current EPA models to adequately track the time-dependence of disease; and

(2) to develop the supporting data needed to define adjustments for potency factors that will allow them to be used with an exposure index that even more closely captures the criteria that determine biological activity than the “interim” index recommended in this document.